Meme Kanseri Hastalarında Kemoterapinin Böbrek Fonksiyonlarına Etkisi

Effect of Chemotherapy on Renal Function Tests of Breast Cancer Patients

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ÖZET

Amaç: Erken meme kanseri olan hastalarda adjuvan kemoterapi ile böbrek fonksiyonlarındaki değişiklikler araştırıldı. **Yöntem:** İnfiltratif duktal karsinomu olan 40 kadın hasta çalışmaya alındı. Kemoterapi (adriamisin + siklofosfamid, veya siklofosfamid + epirubisin veya siklofosfamid + metotreksat + 5-florourasil veya 5-florourasil + epirubisin + siklofosfamid) öncesi ve sonrası serum kreatinin düzeyleri ve MDRD formülü ile hesaplanan glomerül filtrasyon değerleri saptandı. **Sonuçlar:** Tüm hastaların kemoterapi öncesi ortalama serum kreatinin düzeyi 0.69 ± 0.16 ve kemoterapi sonrası ortalama serum kreatinin düzeyi 0.68 ± 0.14 mg/dL olarak saptandı. Hastaların, kemoterapi öncesi ortalama glomerül filtrasyon değeri 99 mL/dk/1.73 m^2 ve kemoterapi sonrası ortalama glomerül filtrasyon değeri 100 mL/dk/1.73 m^2 olarak bulundu ($p>0.05$). **Tartışma:** Sonuç olarak, infiltratif duktal karsinomu olan hastalarda adjuvan kemoterapötik ajanların klinik olarak belirgin nefrotoksik etkilerinin olmadığı belirlendi. Kemoterapötik rejimler arasında serum kreatinin ve glomerül filtrasyon değerleri açısından bir fark saptanmadı.

Anahtar sözcükler: glomerül filtrasyon değeri, serum kreatinin değeri, meme kanseri, adjuvan kemoterapi

ABSTRACT

Aim: We aimed to find out the renal function alteration with respect to adjuvant chemotherapy administration in early breast cancer patients. **Methods:** Forty women with diagnosis of infiltrative ductal carcinoma involved into the study. The data of serum creatinine levels and glomerular filtration rate were collected before chemotherapy and after completing all cycles of different treatment regimens (adriamycin + cyclophosphamide, or cyclophosphamide + epirubicin, or cyclophosphamide + methotrexate + 5-fluorouracil, or 5-fluorouracil + epirubicin + cyclophosphamide). **Results:** The mean creatinine levels of our 40 breast cancer patients were 0.69 ± 0.16, and 0.68 ± 0.14 mg/dL before and after chemotherapy respectively. Mean glomerular filtration rate of our patients were 99 mL/min/1.73 m^2 and 100 mL/min/1.73 m^2 before chemotherapy and after chemotherapy respectively ($p>0.05$). **Conclusion:** The adjuvant chemotherapeutic agents were found not to have any clinically evident nephrotoxic effects. No difference was noticed between chemotherapy regimens with respect to creatinine levels and glomerular filtration rate.

Keywords: glomerular filtration rate, serum creatinine level, breast cancer, adjuvant chemotherapy

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Introduction

Breast cancer is the most common cancer in women and accounts for 29% of all cancers diagnosed each year (1). Adjuvant chemotherapy improves the overall survival of women treated after surgery for early breast cancer. The chemotherapy regimens used for breast cancer including cyclophosphamide, adriamycin, methotrexate, have kidney toxicity (2-4). In clinical practice, nephrotoxicity is measured via creatinine serum values and determination of glomerular filtration rate (GFR). GFR measurement is more sensitive to detect glomerular damage as compared to serum creatinine values.

With this study we aimed to find out the effect of adjuvant chemotherapeutic regimens on renal functions by evaluating the serum creatinine levels and GFR of the breast cancer patients before and after

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chemotherapy. GFR of the patients were calculated by MDRD (modification of diet in renal disease) formula; because calculating GFR with MDRD formula was found to be more accurate than other methods for evaluation of renal functions in cancer patients (5).

Materials and Methods

Forty patients (with a mean age of 55.05±10.58) all of which had diagnosis of breast cancer (infiltrative ductal carcinoma) at our oncology department were included into the study. The data about these patients were evaluated retrospectively. Since this study intended to evaluate the changes in renal functions of breast cancer patients under the effect of chemotherapy, the only inclusion criteria were diagnosis of breast cancer (infiltrative ductal carcinoma) and application of adjuvant chemotherapy. For each patient, data on serum creatinine (measured by kinetic colorimetric assay), stage of malignancy were collected. GFR of patients was calculated by MDRD formula as shown below (6).

GFR: 170 × [Plasmacreatinine]-0.999 × [age]-0.176 × [0.762 if patient is female] × [1.180 if patient is black] × [Serum Urea Nitrogen]-0.170 × [albumin] +0.318.

The creatinine levels before chemotherapy and approximately 3 months after chemotherapy were measured. GFR of the patients before and after chemotherapy were calculated according to their creatinine levels. The chemotherapy regimens were grouped as AC and other regimens (because of heterogenous distribution of the patients).

The paired t test was used for comparison of creatinine and GFR levels before and after chemotherapy, Kruskal-Wallis test was used to compare the changes in creatinine, GFR with chemotherapy according to the stage of the disease. t test was used to compare the changes in creatinine and GFR levels according to the chemotherapy regimen.

Results

The mean creatinine levels of our 40 breast cancer patients were 0.69±0.16, and 0.68±0.14 mg/dL before and after chemotherapy respectively ($p>0.05$). The mean GFR of our patients were 99 mL/min/1.73 m^2 and 100 mL/min/1.73 m^2 before and after chemotherapy respectively ($p>0.05$).

Of the patients, 10% (4/40) were at stage 1, 72.5% (29/40) were at stage 2, 17.5% (7/40) were at stage 3 and there was no patient at stage 4. When renal functions were estimated by calculating GFR using the MDRD formula, 28% of the patients at stage 3 had GFR of less than 60 mL/min/1.73 m^2 even serum creatinine levels were in the normal range. There was no patient with GFR of less than 60 ml/min/1.73 m^2 at stages 1 and 2 (Table I).

Of the 40 patients, 22 of them were given 4 cycles of AC (adriamycin 60 mg/m^2, doxorubicin-,

Table I. Baseline GFR classifications according to the stages of disease

Stages	GFR >90 mL/min/1.73 m^2	90 ≥GFR >60 mL/min/1.73 m^2	60 ≥GFR>30 mL/min/1.73 m^2
Stage 1	65%	35%	0%
Stage 2	65%	35%	0%
Stage 3	42%	29%	29%

Table II. The effect of regimen on creatinine (cre) levels and GFR of the patients

Parameter	AC regimen group	Other regimens group	P value
Cre baseline (mg/dL)	0.69 ± 0.09	0.69 ± 0.21	NS
Cre after chemotherapy (mg/dL)	0.67 ± 0.12	0.69 ± 0.16	NS
GFR baseline (mL/min/1.73 m^2)	97 ± 19	101 ± 26	NS
GFR after chemotherapy (mL/min/1.73 m^2)	101 ± 21	99 ± 26	NS

NS: nonsignificant

cyclophosphamide 600 mg/m^2, one day every three weeks) regimen, rest of them were taken one of the other regimens (4 cycles of EC: epirubicin 100 mg/m^2, cyclophosphamide 600 mg/m^2, one day every three weeks, 6 cycles of CMF: cyclophosphamide 600 mg/m^2, methotrexate 40 mg/m^2, 5-fluorouracil 600 mg/m^2, one day every three weeks, 6 cycles of FEC: 5-Fluorouracil 500 mg/m^2, epirubicin 50 mg/m^2, cyclophosphamide 500 mg/m^2, one day every three weeks) (7). The creatinine and glomerular filtration rates of the patients in the AC regimen and other regimens groups were not statistically different at baseline and after the therapy ($p>0.05$) (Table II).

Discussion

In the present study, we found that serum creatinine levels and GFR of breast cancer patients did not change after chemotherapy. In addition, the adjuvant chemotherapeutic agents were found not to have any clinically evident nephrotoxic effects. No difference was noticed between the chemotherapy regimens with respect to creatinine levels and GFR.

Hurria et al reported that an increase in creatinine levels after chemotherapy was associated with an increased hematological toxicity in elderly breast cancer patients due to decreased clearance of chemotherapeutics (7). In another study, Kralickova et al found that serum creatinine concentrations decreased significantly due to hyperfiltration after doxorubicin-based chemotherapy in 26 breast cancer patients, however increased urinary activity of N-acetyl-beta-D-glucosaminidase, an indicator of renal tubular cell dysfunction, was found after chemotherapy (3). However as far as our knowledge, no study was present showing the GFR and serum creatinine changes with adjuvant chemotherapy in early breast cancer patients. Eventhough, 29% of the patients at stage 3, have baseline GFR below 60 mL/min/1.73 m^2, no significant decrease in GFR was observed after chemotherapy at this stage of breast cancer patients. Still, it is appropriate to calculate GFR for every breast cancer patient with stage 3 before chemotherapy administration even normal creatinine levels observed.

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